Nicholas J. Santoro (Nev. Bar No. 532)
Jason D. Smith (Nev. Bar No. 9691)
SANTORO WHITMIRE, LTD.
10100 W. Charleston Blvd., Suite 250
Las Vegas, Nevada 89135
Tel.: (702) 948-8771
Fax: (702) 948-8773
E-mail: nsantoro@santoronevada.com,
jsmith@santoronevada.com

Christopher N. Sipes (admitted *pro hac vice*)
Einar Stole (admitted *pro hac vice*)
Michael N. Kennedy (admitted *pro hac vice*)
Megan P. Keane (admitted *pro hac vice*)
Eric R. Sonnenschein (admitted *pro hac vice*)
Alaina M. Whitt (admitted *pro hac vice*)
Han Park (admitted *pro hac vice*)
Jordan L. Moran (admitted *pro hac vice*)
COVINGTON & BURLING LLP
One CityCenter, 850 Tenth Street, NW
Washington, DC 20001
Tel.: (202) 662-6000
Fax: (202) 662-6291
E-mail: csipes@cov.com, estole@cov.com,
mkennedy@cov.com, mkeane@cov.com
esonnenschein@cov.com, awhitt@cov.com,
hpark@cov.com, jmoran@cov.com

Attorneys for Plaintiffs Amarin Pharma, Inc. and Amarin Pharmaceuticals Ireland Limited

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEVADA

AMARIN PHARMA, INC. *et al.*, Plaintiffs, v. HIKMA PHARMACEUTICALS USA INC., *et al.*, Defendants.	Case No.: 2:16-cv-02525-MMD-NJK (Consolidated with 2:16-cv-02562-MMD-NJK) **AMARIN'S OPPOSITION TO DEFENDANTS' MOTION FOR SUMMARY JUDGMENT** **ORAL ARGUMENT REQUESTED**

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TABLE OF ABBREVIATIONS

'728 Patent	U.S. Patent No. 8,293,728 (filed Jan. 12, 2012) (Defs.' Ex. 5)
Amarin	Plaintiffs Amarin Pharma, Inc. and Amarin Pharmaceuticals Ireland Limited
ANDA	Abbreviated New Drug Application
apo B	apolipoprotein B
Budoff	Amarin's clinical infringement expert, Matthew Budoff, M.D.
Budoff Opening Rept.	Opening Expert Report of Matthew Budoff, M.D., dated March 10, 2019 (Ex. 9)
Budoff Reply Rept.	Reply Expert Report of Matthew Budoff, M.D., dated June 10, 2019 (Ex. 10)
Defs.' Br.	Defendants' Motion for Summary Judgment of Noninfringement (ECF No. 236)
Defs.' Ex.	exhibit attached to the Declaration of Claire A. Fundakowski (ECF No. 237)
Defendants	Defendants Hikma Pharmaceuticals USA Inc., Hikma Pharmaceuticals International Limited, Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd.
EPA	eicosapentaenoic acid
Ex.	exhibit to Amarin's Opposition to Defendants' Motion for Summary Judgment of Noninfringement
Fisher	Defendants' clinician expert, Edward Fisher, M.D.
FDA	U.S. Food and Drug Administration
Heinecke	Defendants' validity expert, Jay Heinecke, M.D.
LDL-C	low-density lipoprotein cholesterol
Mathers	Defendants' regulatory expert, Peter Mathers
Peck	Amarin's regulatory expert, Carl Peck, M.D.
Peck Rept.	Reply Expert Report of Carl C. Peck, M.D., dated June 10, 2019 (Ex. 12)
Sheinberg	Defendants' clinician expert, Jonathan Sheinberg, M.D.
Sheinberg Rebuttal Rept.	Rebuttal Expert Report of Jonathan I. Sheinberg, M.D., F.A.C.C., on Noninfringement of the Asserted Claims of the Patents-in-Suit, dated May 10, 2019 (Ex. 13)
TG	triglyceride
Vascepa Label	Vascepa Prescribing Information (2017) (Defs.' Ex. 13)

I. INTRODUCTION AND FACTUAL BACKGROUND

Defendants have moved for summary judgment of noninfringement, arguing that Amarin cannot show that, after FDA approval of their ANDAs, Defendants will *induce* infringement of any asserted claim under 35 U.S.C. § 271(b), or *contribute to* infringement of any asserted claim under 35 U.S.C. § 271(c). For the reasons explained below, Defendants' motion should be denied.

Defendants acknowledge that the induced infringement question here turns on how clinicians would understand the instructions for use that accompany Defendants' proposed generic products, known as the "prescribing information" or "label." But Defendants' motion ignores both the plain text of the prescribing information and expert testimony explaining that clinicians would understand the prescribing information to encourage, recommend, or suggest use of their products in ways that infringe the asserted method of treatment claims. Defendants also fundamentally mischaracterize the law of induced and contributory infringement. Defendants suggest that, if a drug's label instructs a range of possible uses (*e.g.*, an indefinite duration of administration), it does not induce any particular use within that range. This is contrary to Federal Circuit precedent: "evidence that the product labeling that Defendants' seek would inevitably lead some physicians to infringe establishes the requisite intent for inducement." *Eli Lilly & Co. v. Teva Parenteral Meds.*, 845 F.3d 1357, 1369 (Fed. Cir. 2017); *see also Vanda Pharms. v. West-Ward Pharms.*, 887 F.3d 1117, 1132 (Fed. Cir. 2018) ("Even if not every practitioner will prescribe an infringing dose, that the target dose range 'instructs users to perform the patented method' is sufficient to 'provide evidence of [West-Ward's] affirmative intent to induce infringement."). Amarin will present expert testimony at trial, including admissions from *Defendants*' experts, establishing that the Federal Circuit's test is met. Defendants invite the Court to disregard that testimony and resolve hotly-disputed factual issues against the non-movant, Amarin. The Court should decline Defendants' invitation and deny this motion.

* * * * *

This Hatch-Waxman patent infringement action arises from Defendants' desire to obtain FDA approval to market generic copies of Amarin's Vascepa product. The active ingredient in Vascepa is a highly purified omega-3 fatty acid called ethyl-eicosapentaenoic acid ("EPA" or

"icosapent ethyl"), and is FDA-approved "to reduce triglyceride (TG) levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia."[1] Vascepa Label, § 1 (Defs.' Ex. 13). While Defendants disparage the invention they seek to copy by observing that "Amarin did not invent purified EPA" (Defs. Br. at 1), Amarin scientists were the first to recognize its utility in treating severe hypertriglyceridemia. Amarin scientists were also the first to recognize EPA's unique ability to treat severe hypertriglyceridemia while avoiding the adverse effects associated with prior therapies, such as a substantial rise in LDL-C (the so-called "bad cholesterol) that accompanied the reduction in TGs in those therapies. As Defendants' own experts concede, Vascepa was the first, and remains the only, product approved for the treatment of severe hypertriglyceridemia that reduces triglycerides without raising LDL-C. *See* Heinecke Deposition Tr. 143:9–144:10 (Ex. 2); Fisher Dep Tr. 271:23–272:8 (Ex. 3).

Indeed, in the pivotal 12-week, double-blind "MARINE" clinical trial supporting approval of Vascepa®, Vascepa was shown to both avoid an increase in LDL-C and actually reduce apo B (a measure of the number of pro-atherogenic particles in the blood). *See* Vascepa Label, § 14. And, as a result of the recent REDUCE-IT cardiovascular outcome trial, Vascepa is the only drug approved for treatment of severe hypertriglyceridemia that has also been shown to provide cardiovascular benefit to patients on top of a statin. Heinecke Tr. 147:7-13.

The learnings from the MARINE trial form the basis for the prescribing information (or label) at the heart of Defendants' Motion. That prescribing information informs clinicians how to safely and effectively use Vascepa to treat their patients with severe hypertriglyceridemia, and what clinically meaningful effects to expect. Several aspects of the label are relevant to this motion. For example, the "Indications and Usage" section states that Vascepa is indicated "to reduce triglyceride (TG) levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia." Vascepa Label, § 1.

[1] "Hypertriglyceridemia" refers to elevated triglyceride levels in the blood. Elevated TG levels are associated with several diseases and disorders, including pancreatitis and cardiovascular disease. Hypertriglyceridemia patients are divided into three classes based on the level of TGs: borderline high (150–199 mg/dl), high (200–499 mg/dl), and severe (≥ 500 mg/dl).

The "Dosage and Administration" section states that "[t]he daily dose of VASCEPA is 4 grams per day." Vascepa Label,§ 2. The "Clinical Studies" section describes the results of the MARINE trial, including how the patients' lipid levels were affected by 12 weeks of treatment with Vascepa:

Table 2. Median Baseline and Percent Change from Baseline in Lipid Parameters in Patients with Severe Hypertriglyceridemia (≥500 mg/dL)

	VASCEPA 4 g/day N=76		Placebo N=75		Difference (95% Confidence
Parameter	Baseline	% Change	Baseline	% Change	Interval)
TG (mg/dL)	680	-27	703	+10	-33* (-47, -22)
LDL-C (mg/dL)	91	-5	86	-3	-2 (-13, +8)
Non-HDL-C (mg/dL)	225	-8	229	+8	-18 (-25, -11)
TC (mg/dL)	254	-7	256	+8	-16 (-22, -11)
HDL-C (mg/dL)	27	-4	27	0	-4 (-9, +2)
VLDL-C (mg/dL)	123	-20	124	+14	-29** (-43, -14)
Apo B (mg/dL)	121	-4	118	+4	-9** (-14, -3)

% Change= Median Percent Change from Baseline
Difference= Median of [VASCEPA % Change – Placebo % Change] (Hodges-Lehmann Estimate)
p-values from Wilcoxon rank-sum test
*p-value < 0.001 (primary efficacy endpoint)
**p-value < 0.05 (key secondary efficacy endpoints determined to be statistically significant according to the pre-specified multiple comparison procedure)

Vascepa Label, § 14 (annotations added). As shown here, patients' TG levels were reduced 27% compared to baseline and 33% compared to placebo; their LDL-C levels were reduced 5% compared to baseline and 2% compared to placebo; and their apo B levels were reduced 4% compared to baseline and 9% compared to placebo. The Clinical Studies section further states that "The reduction in TG observed with VASCEPA was not associated with elevations in LDL-C levels relative to placebo." Vascepa Label, § 14.

The 15 asserted patent claims,[2] *see* Appendix A, are all drawn to methods of treating patients with severe hypertriglyceridemia by administering 4 grams of EPA, consistent with the Vascepa label. Each asserted claim further tracks the approved Vascepa label by requiring treatment for at least 12 weeks, as disclosed in the Clinical Studies section. The label also comes with a patient information leaflet that instructs patients "[d]o not . . . stop taking VASCEPA without talking to your

[2] Amarin is asserting the following claims in this case: Claims 1, 13, and 16 of the '728 Patent (Defs.' Ex. 5); Claim 14 of the '715 Patent (Defs.' Ex. 6); Claims 1, 7 and 8 of the '677 Patent (Defs.' Ex. 7); Claims 1, 7, and 8 of the '652 Patent (Defs.' Ex. 8); Claims 4, 7, and 17 of the '560 Patent (Defs.' Ex. 9); and Claims 1 and 5 of the '929 Patent (Defs.' Ex. 10).

doctor." Vascepa Label, at 9–10. Both sides' clinician experts agree that indefinite (i.e., enduring) treatment is required for the vast majority of patients with severe hypertriglyceridemia in order to keep their TG levels below 500 mg/dL. Therefore, when prescribing Vascepa according to the label, clinicians expect and intend that their patients will be on the medication for more than 12 weeks, as Defendants' experts concede. *See, e.g.,* Fisher Tr. 72:14 ("one way of phrasing [the indication] is for the duration; meaning longer than 12 weeks."). Many of the asserted claims are also drawn to methods of treatment that avoid rises in LDL-C or reduce apo B, capturing the benefits of the claimed treatment observed in the MARINE study.

As Defendants acknowledge, their proposed labels—which are included as part of their ANDAs pending with FDA—are "materially identical to the Vascepa label." Defs.' Br. at 12 n.18.[3] In fact, Defendants' regulatory expert agreed that "defendants did not change or omit any material information from the Vascepa labeling in drafting their own proposed labeling," Mathers Tr. 36:10–14 (Ex. 4); *see also id.* at 33:8–34:2 (agreeing that the Defendants' labels and the Vascepa label are identical). It is worth noting that FDA provides avenues for generic ANDA filers to attempt to deviate in certain respects from the relevant branded product's prescribing information. *See* Mathers Tr. 37:3–17; *see also* 21 C.F.R. § 314.92(a)(1) ("[C]onditions of use for which approval cannot be granted because of . . . an existing patent may be omitted [from a generic product's label]."). Defendants here have chosen to copy Vascepa's label.

II. SUMMARY OF THE ARGUMENT

By seeking approval for a "bioequivalent" product and copying Vascepa's label as their own, Defendants thus represent to FDA, clinicians, and patients that the same clinical effects achieved with Vascepa will also be achieved with their products. Because the Vascepa and Defendants' labels instruct physicians to use the product according to the asserted claims in carrying out the safe and effective use of the product, Defendants induce infringement of the claims: "[E]vidence that the product labeling that Defendants seek would inevitably lead some physicians to infringe establishes

[3] For this reason, like Defendants' brief, Amarin's brief also cites to the Vascepa label.

the requisite intent for inducement." *Eli Lilly*, 845 F.3d at 1369; *see also AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010). Nevertheless, Defendants' motion seeks various escape hatches to avoid a finding of infringement. No such escape hatch exists.

First, with respect to inducement, Defendants acknowledge that the question of their intent revolves around their proposed prescribing information. *See, e.g.*, Defs.' Br. at 8–9. But Defendants' selective reading of that labeling directly conflicts with Federal Circuit precedent. In Hatch-Waxman cases where, as here, a generic ANDA filer is accused of inducing infringement of a method of treatment patent, intent to induce infringement is established when "the label, *taken in its entirety*" "recommend[s] or suggest[s] *to a physician*" that the drug used in the claimed method of treatment is safe and effective for causing the combination of effects described in the patent claims. *Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316, 1324 (Fed. Cir. 2012) (emphases added). Thus, Defendants cannot ignore aspects of the label, such as the Clinical Studies section, that help establish their intent to induce. *See, e.g.*, *Sanofi v. Watson Labs. Inc.*, 875 F.3d 636, 645–46 (Fed. Cir. 2017) (relying on the Clinical Studies section of the label); *Vanda*, 887 F.3d at 1131 (relying on the Pharmacokinetics section of the label). *See, e.g.*, *infra* Section V.A.2. Here, the labels taken as a whole instruct physicians that the product may be administered to a patient for 12 weeks or more so as to reduce her TGs without increasing LDL-C, and need not be co-administered with a lipid-altering drug to control LDL-C levels. And under Federal Circuit law, the label's direction of infringing use establishes intent *regardless of* whether the odd patient discontinues treatment prematurely, or chooses to use the product with a statin. *See infra* Section V.A.

The Federal Circuit has also recognized that expert testimony establishing how clinicians interpret the label is critical in the induced infringement analysis. *Bayer*, 676 F.3d at 1324; *see also, e.g.*, *Vanda*, 887 F.3d at 1131 (affirming a finding of induced infringement based on expert testimony to explain that the "laboratory tests" described in the product label referred to the "genotyping tests" described in the patent claims). Here, the parties' experts agree that physicians consider prescribing information as a whole in making prescribing judgments. Budoff Tr. 127:14–22 (Ex. 5); Mathers Tr. 117:4–8; Peck Tr. 142:10–22 (Ex. 6). Moreover, Defendants' clinical expert, Dr. Sheinberg, agreed

that [redacted] Sheinberg Tr. 227:13–22 (Ex. 7). Granting Defendants' motion would require simply ignoring this expert testimony which, at minimum, establishes genuine issues of material fact concerning Defendants' intent to induce. *See infra* Section V.

Second, Defendants repeatedly assert that Plaintiffs' contributory infringement claims fail because Defendants' generic products are "suitable for substantial noninfringing use." *See, e.g.*, Defs.' Br. at 18. Defendants would erase the word "substantial" from the legal standard, asserting that any conceivable noninfringing use precludes contributory infringement. But determining whether a noninfringing use is "substantial" involves consideration of "not only the use's frequency, but also the use's practicality, the invention's intended purpose, and the intended market." *i4i Ltd. P'ship v. Microsoft Corp.*, 598 F.3d 831, 851 (Fed. Cir. 2010). Here, Defendants cannot show that the non-infringing use meets any of these criteria. *See infra* Section VI.

III. STATEMENT OF UNDISPUTED AND DISPUTED MATERIAL FACTS

A. Response to Defendants' Statement of Undisputed Facts

Defendants' statement of "undisputed material facts," Defs.' Br. at 6–8, contains facts wrongly identified as "undisputed," while omitting other allegedly undisputed facts upon which they appear to rely, in violation of Local Rule 56-1.[4] Defendants' "undisputed material facts" are disputed as follows:

Response to Defendants' ¶ 1a: Amarin agrees that "[e]ach of the 15 asserted claims requires

[4] Defendants appear to rely on at least the following purported facts missing from their statement of undisputed material facts: (1) "The 'Clinical Studies' section of the label . . . merely describes exemplary effects of the drug, as opposed to the 'Indications and Usage' or 'Dosage and Administration' sections, which instruct how to use it." Defs.' Br. at 12; (2) "'some physicians will find some of the data in the clinical studies is helpful, [others] will find it irrelevant to their practices.'" *Id.*; (3) "those median numbers—i.e., the overall midpoints of the values reported for the [MARINE] study's 76 patients—do not predict icosapent's effects in a real-world patient, or even in the individual patients in the study." Defs.' Br. at 19; (4) "In practice, it is even less common [than 25%] for patients to receive Vascepa without concurrent statin therapy." Defs.' Br. at 26.

administering icosapent to a patient" *with severe hypertriglyceridemia* (TG ≥500 mg/dL) "for at least '12 weeks.'"

Response to Defendants' ¶ 1b: Amarin does not dispute that fourteen of the asserted claims "further require at least one of the following effects: (i) a reduction in triglycerides that is 'statistically significant' or 'of at least about' 10%, 20%, or 25%; (ii) no increase, no 'substantial[]' increase, no 'statistically significant' increase, or no 'more than 5%' increase in LDL-C levels; or (iii) a reduction in 'apolipoprotein B.'"

Response to Defendants' ¶ 1c: Amarin does not dispute that "[f]our asserted claims require that the patient 'not receive concurrent lipid altering therapy,' e.g., a statin."

Response to Defendants' ¶ 1d: Amarin agrees that the specification in the asserted patents states that TG reduction can occur in a shorter period of time than 12 weeks. However, maintaining that reduction in severely hypertriglyceridemic patients requires enduring treatment that generally continues for well beyond 12 weeks, and the patent specification (e.g., in the Patent Example), describes treatment of severely hypertriglyceridemic patients for 12 weeks and more. *See* '728 Patent, at 13:26–34, 14:61–63 (Defs.' Ex. 5).

Response to Defendants' ¶ 2a: Amarin agrees that the MARINE Clinical Study Report states that for the group of subjects receiving 4 g of Vascepa per day, "the maximum effect on fasting TG reduction occurred by Week 4." And that "[f]rom Week 4 to Week 12, the TG-lowering effects were maintained in the . . . 4 g group[] while TG levels increased in the placebo group." Defs.' Ex. 11 (FDA Medical Review for Vascepa) at 67. Only the 12-week results, and not the 4-week results, appear in the product labels. Vascepa Label, § 14; *see also* Mathers Tr. 96:23-97:8.

Response to Defendants' ¶ 2b: Amarin agrees that the MARINE Clinical Study reported that "about 21% of patients" in the placebo group achieved an endpoint TG of <500 mg/dL. Amarin disputes that these patients "kept triglyceride levels from becoming 'very high' with diet and exercise alone." Patients with baseline TG <500 mg/dL were ineligible to be included in the study.

Responses to Defendants' ¶¶ 2c–e: Amarin agrees that the MARINE Clinical Study reported that the third quartile of patients in the 4 g treatment arm showed "no reduction in triglycerides," "a

greater-than-5% increase in LDL-C", and a 3.8% "increase in Apo B." MARINE further reported median reductions in TGs of 27% and 33%, LDL-C of 5% and 2%, and apo B of 4% and 8.5%, compared to baseline and placebo, respectively.

Response to Defendants' ¶ 2f: Amarin does not dispute that the MARINE Clinical Study reported that "[a]bout 25% of patients concurrently received a statin while on Vascepa therapy."

Response to Defendants' ¶ 3a: Amarin does not dispute that Defendants' proposed product labels "[a]re indicated solely 'as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.'"

Response to Defendants' ¶ 3b: Amarin disputes that Defendants' proposed product labels "have 'no explicit instruction . . . to use the drug for at least 12 weeks.'" For example, as Amarin's clinician expert noted, [redacted] Budoff Tr. 200:2–5; Budoff Opening Rept.[5] ¶ 127 (Ex. 9); Budoff Reply Rept. ¶¶ 66–71 (Ex. 10); Peck Tr. 148:4–12, and the clinical studies section [redacted] Budoff Tr. 146:6–15. *See also* Budoff Opening Rept. ¶¶ 123–26; Budoff Reply Rept. ¶¶ 43–58 [redacted]

Response to Defendants' ¶ 3c: Amarin agrees that the Clinical Studies Section of Defendants' proposed product label informs clinicians that 25% of patients receiving Vascepa in the MARINE study were "concurrently receiving a statin," and thus necessarily informs clinicians that 75% of patients were not concurrently receiving a statin. Mathers Tr. 68:1–12. Defendants' regulatory expert, Mr. Mathers, acknowledged that Vascepa is approved for the treatment of severely hypertriglyceridemic patients who are not receiving other lipid-altering drugs (such as a statin), *id.* at

[5]Dr. Budoff's Opening Expert Reports addressing DRL's ANDA Product are the same in all material respects to the statements and opinions in Dr. Budoff's Opening Expert Report addressing Hikma's ANDA Product. Budoff Decl. ¶ 4 (Ex. 8). Thus, although this brief cites to Dr. Budoff's Hikma report, the statements referenced apply equally to both Hikma's and DRL's infringement.

67:5–14, and that the Clinical Studies section of the Vascepa label informs clinicians that the drug is safe and effective for patients who are not receiving concomitant statin therapy or other lipid-altering medication, *id.* at 76:10–18.

B. Plaintiffs' Statement of Additional Undisputed Facts

1. All fifteen of the asserted patent claims are directed to the treatment of severe hypertriglyceridemia. *See* Appendix A (all claims directed to treatment of patients with fasting baseline TG levels of 500 mg/dl or greater).

2. Severe hypertriglyceridemia is a chronic condition. *See, e.g.*, Sheinberg Tr. 143:22–25; Budoff Tr. 194:12–22; *id.* at 203:15–19; Budoff Reply Rept. ¶¶ 46–65; Peck Tr. 136:7–9.

3. Most clinicians who treat severely hypertriglyceridemic patients with Vascepa will administer the drug for 12 weeks or more. Budoff Tr. 90:13–15; Sheinberg Tr. 134:21–135:5; Budoff Opening Rept. ¶ 123; Budoff Reply Rept. ¶ 49.

4. There are no differences between the Vascepa label and Defendants' labels that are material to induced infringement. Defs.' Br. at 12 n.18; Mathers Tr. 33:8–34:2.

5. Defendants did not seek to omit any information in the Vascepa label from their own labels. Mathers Tr. 36:10–14.

6. The Vascepa label reports a median reduction in TGs of at least about 25%, a median reduction in apo B, and a median reduction in LDL-C, compared to both baseline and placebo and expressly states that "the reduction in TG observed with VASCEPA was not associated with elevations in LDL-C levels relative to placebo." *See* Vascepa Label, § 14.

IV. SUMMARY JUDGMENT LEGAL STANDARD

Summary judgment is proper only when the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). A genuine dispute exists whenever there is a sufficient evidentiary basis on which a reasonable fact-finder could rely to find for the nonmoving party. *See Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986). "The amount of evidence necessary to raise a genuine issue

of material fact is enough 'to require a jury or judge to resolve the parties' differing versions of the truth at trial.'" *Aydin Corp. v. Loral Corp.*, 718 F.2d 897, 902 (9th Cir. 1983) (quoting *First Nat'l Bank v. Cities Serv. Co.*, 391 U.S. 253, 288–89 (1968)). At summary judgment, a court's function is not to weigh the evidence and determine the truth, but to determine whether there is a genuine issue for trial. *See Anderson*, 477 U.S. at 249. Indeed, at summary judgment the evidence of the nonmovant is "to be believed, and all justifiable inferences are to be drawn in his favor." *Anderson*, 477 U.S. at 255.

V. FACT ISSUES REMAIN FOR TRIAL ON AMARIN'S INDUCED INFRINGEMENT CLAIMS

Anyone who "actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b). Establishing inducement requires evidence showing that the accused infringer "possessed specific intent to encourage another's infringement." *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006). "Infringement is a question of fact."[6] *AstraZeneca v. Apotex*, 633 F.3d at 1056. In a Hatch-Waxman case, the intent prong is shown so long as the product label, read as a whole, encourages, promotes, recommends, or suggests that clinicians use the generic product in a manner that infringes the patent. *Vanda*, 887 F.3d at 1129; *Bayer*, 676 F.3d at 1324; *see also Takeda Pharm. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015) (active inducement shown when the label "suggest[s] that an infringing use 'should' be performed"). "In sum, evidence that the product labeling that Defendants seek would inevitably lead some physicians to infringe establishes the requisite intent for inducement." *Eli Lilly*, 845 F.3d at 1369.

Contrary to Defendants' implication, *see* Defs.' Br. at 10 n.17, courts frequently decline to conclude as a matter of law that a generic ANDA filer's label does not induce infringement.[7] In fact,

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[6] Defendants incorrectly contend that Plaintiffs must carry a "heavy burden" of showing induced and contributory infringement. *See, e.g.*, Defs.' Br. at 15. At trial, Amarin bears the burden of proving infringement by a mere *preponderance* of the evidence. *Vanda*, 887 F.3d at 1125. This burden is no "heav[ier]" because Amarin is pursuing induced and contributory infringement.

[7] *See Impax Labs., Inc. v. Actavis Labs. FL, Inc.*, No. CV 15-6934 (SRC), 2018 WL 1863826, at *10 (D.N.J. Apr. 18, 2018) (denying defendant's motion for summary judgment because the question of (continued…)

it is only when "the label, *taken in its entirety*, fails to recommend or suggest *to a physician* that [the drug] is safe and effective for inducing the claimed combination of effects in patients" is intent to induce infringement lacking. *Bayer*, 676 F.3d at 1324 (emphases added). As the phrase "the label, taken in its entirety" implies, the inquiry is not limited to the Indications and Usage section.[8] Moreover, determining what a product label "recommend[s] or suggest[s] to a physician" requires reading the product label from the viewpoint of the clinician. *Bayer*, 676 F.3d at 1324; *see also Vanda*, 887 F.3d at 1131 (citing expert testimony that clinicians read "laboratory tests" in the product label as encouraging clinicians to perform the "genotyping tests" described in the asserted patent claims).

A. Defendants' Product Labels Will Induce Clinicians to Administer Their Generic Products to Severely Hypertriglyceridemic Patients for At Least 12 Weeks

The asserted patent claims describe a method of treating severe hypertriglyceridemia by administering 4 grams per day of purified EPA for at least 12 weeks. Amarin will show at trial that clinicians will read Defendants' product labels as a whole—the "Indications and Usage" and

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specific intent to induce infringement is a question for the finder of fact); *GlaxoSmithKline LLC v. Glenmark Pharm. Inc.*, No. CV 14-877-LPS-CJB, 2017 WL 8948973, at *17 (D. Del. May 23, 2017), report and recommendation adopted, No. CV 14-877-LPS-CJB, 2017 WL 2536431 (D. Del. June 9, 2017) (denying defendants' motion for summary judgment where a factfinder could reasonably conclude that doctors would interpret the labels as instructing use consistent with the asserted patent claims); *see also Bio Tech. Gen. Corp. v. Duramed Pharm., Inc.*, 325 F.3d 1356 (Fed. Cir. 2003) (reversing the grant of summary judgment and remanding for factual determination of whether consumers using product in accordance with package instructions would infringe patent); *Allergan Sales, LLC v. Sandoz, Inc.*, 211 F. Supp. 3d 907, 923 (E.D. Tex. 2016), aff'd in part, rev'd in part, 717 F. App'x 991 (Fed. Cir. 2017) (denying motion for summary judgment of noninfringement because genuine disputes of material fact remained whether defendant's label encouraged infringement); *Genentech, Inc. v. Trustees of Univ. of Penn.*, 871 F. Supp. 2d 963, 977 (N.D. Cal. 2012) (same); *Wyeth v. Sandoz, Inc.*, 703 F. Supp. 2d 508, 523 (E.D.N.C. 2010) (same).

[8] *See, e.g.*, *Bayer*, 676 F.3d at 1324 (considering what "the label, taken in its entirety" recommends or suggests to a physician); *see also Vanda*, 887 F.3d at 1131 (relying on the Pharmacokinetics section of the product label), *Sanofi v. Watson*, 875 F.3d at 645–46 (relying on the Clinical Studies section of the product label), *Pernix Ireland Pain DAC v. Alvogen Malta Operations Ltd.*, 323 F. Supp. 3d 566, 585–86 (D. Del. 2018) (Bryson, J.) (relying on the Pharmacokinetics section and "dosing instructions and clinical data" in the product label).

"Clinical Studies" sections in particular—as encouraging, suggesting, or recommending use of 4 grams per day of Defendants' generic products for at least 12 weeks. *See, e.g.*, Budoff Opening Rept. ¶¶ 122–128; Budoff Reply Rept. ¶¶ 39–87; Peck Rept. ¶¶ 166–203 (Ex. 12). Defendants are of the contrary opinion (Defs.' Br at 11), but their argument ignores the Federal Circuit's directive to consider what "the label, taken in its entirety" recommends or suggests to clinicians. *See Bayer*, 676 F.3d at 1324. Amarin will show that a clinician, understanding that severe hypertriglyceridemia is a chronic condition, would understand the indication in the label to refer to indefinite treatment, and would understand the clinical studies portion of the label to convey that treatment would need to last for at least 12 weeks. A finding of infringement would be perfectly in line with Federal Circuit cases considering similar patents and similar labeling. Both sides' experts agreed with the essential aspects of this argument, which utterly precludes summary judgment. Defendants ignore or discount all of this evidence.

Defendants' faulty logic is illustrated by the reasoning in a recent district court opinion which found infringement on strikingly similar facts, with respect to a claim directed to treatment "for at least 12 months." *Sanofi v. Glenmark Pharmaceuticals Inc., USA*, 204 F. Supp. 3d 665, 683–84 (D. Del. 2016), *aff'd*, 875 F.3d 636 (Fed. Cir. 2017). There, as here, the Indications and Usage section of the labels did not limit the duration of the treatment. *Id.* at 683. There, as here, expert testimony established that the indicated use was for a "chronic disorder" for which clinicians intended administration of the drug "indefinitely." *Id.* There, as here, the label reported a clinical trial and the length of that trial would further encourage clinicians to administer for at least the claimed duration of 12 months. *Id.* at 683–84. The same result should be reached here with respect to the "12 weeks" limitations. At an absolute minimum, there is a genuine dispute of material fact as to whether the label encourages, recommends, or suggests that clinicians administer Defendants' products for 12 weeks, thus precluding a ruling that Defendants lack intent to induce as a matter of law.

1. Clinicians Understand the Indications and Usage Section to Encourage, Recommend, or Suggest the Use of Defendants' ANDA Products for at Least 12 Weeks

The Indications and Usage section of Defendants' product labels, by itself, will inevitably

lead some clinicians to infringe, thus establishing the requisite intent to induce clinicians' infringement. The record evidence, including admissions from Defendants' experts, shows that the clear majority of clinicians who prescribe Vascepa in accordance with Defendants' labels will, as a result, administer Vascepa to their severely hypertriglyceridemic patients for far longer than 12 weeks. Defendants' attempt to refute this proposition is unsupported by evidence, much less evidence that would be sufficient to resolve the issue against Amarin *as a matter of law*.

The Indications and Usage section states that Defendants' generic products will be "indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia." Vascepa Label, § 1; *see also* Budoff Reply Rept. ¶¶ 47–48. Unlike with some other approved drugs, there is no time limit on how long a clinician is to administer Vascepa.[9]

[redacted] Budoff Tr. 194:12–22; *see also* Budoff Opening Rept. ¶ 23; Budoff Reply Rept. ¶¶ 46–65; Peck Rept. ¶¶ 130, 170–75.

And this is for good reason—both sides' experts also agree that severe hypertriglyceridemia is a chronic condition, which informs how a clinician would interpret the lack of a time limit on administration in the Indications and Usage section. Budoff Tr. 203:17–19 [redacted] Defendants' clinician expert, Dr. Sheinberg, explains: [redacted] Sheinberg Tr. 143:22–25 (emphasis added). Amarin's clinical expert agrees that severe hypertriglyceridemia is a chronic disease. Budoff Tr. 194:12–22; *see also* Budoff Reply Rept. ¶ 49; Peck Tr. 136:7–9. And, as a chronic condition, physicians would also understand that if a severely hypertriglyceridemic patient stops treatment, their TG levels will return back to pretreatment

[9] When a drug is meant for other than long-term treatment, the product labels for those drugs provide a specific length of treatment. Budoff Reply Rept. ¶¶ 59–63 [redacted] *see also* Peck Rept. ¶ 178.

("baseline") levels. Budoff Tr. 93:23–25 [redacted]; Sheinberg Tr. 144:16–25 [redacted] In recognition of the need for long-term therapy, the Patient Information leaflet attached to Defendants' product labels states: "Do not . . . stop taking VASCEPA without talking to your doctor."[10] Vascepa Label, at 9–10; *see also* Peck Tr. 138:9–14; Peck Rept. ¶ 193.

These facts, upon which both sides' experts agree, establish that clinicians would read the Indication and Usage section as conveying that Vascepa is approved as safe and effective to reduce patients' TG levels to below 500 mg/dl and *keep them there*. Fisher Tr. 72:3–8; *see also id.* 67:18–24; *see also* Budoff Reply Rept. ¶ 44; Peck Tr. 54:1–8; Peck Rept. ¶ 196. Both sides experts agree that most prescribers would understand this to require more than 12 weeks of Vascepa. Defendants' expert, Dr. Fisher, for example, when asked how long most doctors would follow the approved Indication and keep their patient on Vascepa, answered "for the duration; meaning longer than 12 weeks." Fisher Tr. 72:9-15. Thus, to avoid a regression back to their pretreatment levels, clinicians administer the medication indefinitely. Indeed, Dr. Sheinberg emphasized [redacted] Sheinberg Tr. 139:20–21, 141:20-24. Clinicians therefore understand the approved indication for Vascepa to generally require administration for 12 weeks or more in order to reduce triglycerides below 500 mg/dl and keep them there.

Unsurprisingly, then, indefinite administration (i.e., at least 12 weeks of Vascepa) represents how both sides' clinical experts treat their own patients. As Dr. Sheinberg explains, [redacted]

[10] Defendants' expert Mr. Mathers noted that the Vascepa Patient Information leaflet is not "separate" from the label, Mathers Tr. 125:9–126:1, and can be "taken into account in a prescribing decision," Mathers Tr. 122:11–123:15.

[redacted] Sheinberg Rebuttal Rept. ¶ 119 (Ex. 13); *see also* Budoff Reply Rept. ¶ 49.[11] Dr. Sheinberg also testified that [redacted] Sheinberg Tr. 135:3–15. In fact, only in rare circumstances would patients use Defendants' generic products for a short term, and in those cases [redacted] Budoff Tr. 111:7–25. That clinicians read the indication as encouraging long-term treatment (for at least 12 weeks) is also shown by the widespread clinical practice of prescribing patients three to four months of Vascepa at a time and scheduling a follow-up appointment with the patient at least three months after initiating Vascepa therapy. Sheinberg Tr. 233:18–234:6 [redacted] Sheinberg Tr. 139:21–25 [redacted] Budoff Tr. 114:24–25 [redacted] Budoff Opening Rept. ¶¶ 124–26; Budoff Reply Rept. ¶ 52.

Against this backdrop, Defendants' insistence that "the labels never characterize severe hypertriglyceridemia as a chronic condition," Defs.' Br. at 11, falls flat. As does Defendants' contention that the Court should ignore "[i]nformation outside the label." *Id.* at 13. It is well-established, in Federal Circuit law (*see supra* Section II) and in common sense, that clinicians do not read prescribing information in a vacuum, but [redacted] Sheinberg Tr. 227:13–22; *see also* Sheinberg Rebuttal Rept. ¶ 98 [redacted] Budoff Reply Rept. ¶ 37. In fact, this case has more compelling evidence that Defendants intend to induce clinicians' infringement than the court had in

[11] *See also* Budoff Tr. 90:13–15 [redacted] Sheinberg Tr. 134:21–135:5 [redacted] Budoff Reply Rept. ¶ 49.

Sanofi v. Glenmark. There, as here, the court in *Sanofi* was presented with an indication that did not limit the duration and expert testimony that clinicians generally intend indefinite administration. 204 F. Supp. 3d at 683 (finding induced infringement). But here, experts have further testified that the indication itself teaches keeping TGs below 500 mg/dl, which will require more than 12 weeks administration. *See* Fisher Tr. 72:4–8.; *see also id.* 67:18–24.

The Federal Circuit has likewise relied on clinicians' background knowledge in this context. For example, in *Vanda*, the asserted method claim required "performing or having performed a genotyping assay on the biological sample." 887 F.3d at 1121. Although the label at issue in *Vanda* did not literally refer to "a genotyping assay," the Federal Circuit affirmed the district court's reliance on expert testimony to conclude that "when the label states that 'laboratory tests' are available to identify poor metabolizers, the label is referring to 'genotyping tests.'" *Id.* at 1131. Under Defendants' view, the patent holder in *Vanda* would have been out of luck because the label did not use the exact words "genotyping assay." Obviously, that is not the law.

Nor can Defendants avoid infringement because the label does not specifically exclude the possibility that a clinician or patient might choose to discontinue use before 12 weeks and still be within the contours of the indication. *See* Defs.' Br. at 7, 11. This possibility is entirely consistent with a finding of inducement under the governing legal standard, which provides that the "requisite intent for inducement" is established when "the product labeling that Defendants seek would inevitably lead ***some*** physicians to infringe." *Eli Lilly*, 845 F.3d at 1369 (emphasis added). Not that it matters in light of this precedent, but the evidence here shows that, in reality, [redacted] Budoff Tr. 200:23–201:1. Dr. Sheinberg agreed [redacted] Sheinberg Tr. 135:3–15.

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If Defendants genuinely believed that severe hypertriglyceridemia could be successfully treated in less than 12 weeks, they could have petitioned FDA to approve labeling that excluded

administration for 12 weeks or more. *See* 21 C.F.R. § 314.92(a)(1); *see also* Mathers Tr. 37:3–17. There is no evidence in the record that either Defendant has ever sought to do so. The Court is entitled to take this into account as part of the intent inquiry. *See AstraZeneca v. Apotex*, 633 F.3d at 1058 (affirming the district court's induced infringement finding where, despite being aware of infringement issues presented by its label, Apotex proceeded with its plans to distribute its generic drug product without revising the label to avoid infringement). In any event, the record evidence precludes any finding, much less *as a matter of law*, that the Indication and Usage section does not instruct using Vascepa for at least 12 weeks.

2. The Clinical Studies Section Further Encourages, Recommends, or Suggests that Clinicians Use Defendants' Generic Products for at Least 12 Weeks

The data reported in the Clinical Studies section resulted from the MARINE trial, which cost Amarin tens of millions of dollars to conduct over a period of years. And while Defendants now deprecate the data's value to physicians, *see* Defs.' Br. at 12–13, both sides' experts agree that the Clinical Studies section of a label serves a critical role when clinicians make their treating decisions.[12] FDA, for example, explains that this section of the label is meant to provide "concise, accurate summaries of information from studies concerning a drug's effectiveness (and sometimes safety) *that practitioners consider important to clinical decision making*." FDA, *Guidance for Industry: Clinical Studies Section of Labeling for Human Prescription Drug and Biological Products — Content and Format*, at 2 (January 2006), https://www.fda.gov/media/72140/download (Ex. 14) (emphasis added); *see* 21 C.F.R. § 201.57(c)(15) ("Th[e Clinical Studies] section must discuss those clinical studies that facilitate an understanding of how to use the drug safely and effectively."); *see also* Peck Rept. ¶¶ 154–158. In view of FDA's guidance, the fact that the MARINE data is included in the Vascepa labeling signifies that the data is important for clinicians to consider.

[12] *See* Sheinberg Tr. 152:16–153:2, 184:8–22; Mathers Tr. 135:5–18, 170:3–7; Budoff Tr. 146:6–15, 203:4–19; Peck Tr. 124:21–125:4, 133:3–11. Heinecke Tr. 344:22–345:3 (testimony from another of Defendants' clinician experts that the Lovaza label teaches clinicians that treatment with Lovaza will likely lead to a large increase in severely hypertriglyceridemic patients' LDL-C).

The MARINE data describe the effects that patients experienced after 12 weeks of treatment with Vascepa. Vascepa Label, § 14. With that in mind, both sides' experts agree that this section encourages, recommends, or suggests to clinicians that they treat their severely hypertriglyceridemic patients with the product for at least 12 weeks. *See* Mathers Tr. 82:10–15; Budoff Tr. 192:24–193:5, 203:4–19; Budoff Opening Rept. ¶ 127; Budoff Reply Rept. ¶¶ 66–71; Peck Tr. 124:16–125:4, 147:4–16; Peck Rept. ¶¶ 186–92. Thus, the Court should conclude that a clinician would understand that the Clinical Studies section confirms that the label directs at least 12 weeks of use.[13]

Defendants seek to deny the import of the Clinical Studies section by arguing that the data describes only an "infringing mode" for their product, as opposed to a suggestion to a clinician to treat for at least 12 weeks to achieve the described effects. Defs.' Br. at 12. There is no support in either the record or Federal Circuit precedent for this reading. Even *Takeda v. West-Ward*, on which Defendants rely, did not hold that the product label merely described a possible infringing use. Rather, the issue there was a mismatch between the patented method, directed to treating "acute gout," and the product's indication which was directed to "prophylaxis of gout" (*i.e.*, preventing gout, not treating acute gout). *Takeda*, 785 F.3d at 630. The label's only arguable reference to acute gout was an instruction that "[i]f you have a gout flare while taking [the product], tell your healthcare provider." *Id.* Considering a motion for a preliminary injunction (not a summary judgment motion), the Court refused to accept this "vague language" as sufficient to "infer from those instructions an affirmative intent to infringe the patent." *Id.* at 631, 632; *see also Eli Lilly*, 845 F.3d at 1369 (describing the label in *Takeda* as only "tenuously related to the use covered by the asserted claims"). But here, the Clinical Studies section expressly discusses a 12-week course of treatment. Combined with a physician's understanding that the indication is to treat a chronic condition, this constitutes clear direction to treat for at least 12 weeks. *See Sanofi*, 204 F. Supp. 2d at 683.

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[13] Other sections of the label also encourage long-term use of the drug, including the description of "2-year" and "6-month" carcinogenicity studies in the Nonclinical Toxicology Section, Vascepa Label, § 13.1, and the express instruction to patients not to stop taking the medication without talking to their doctor in the Patient Information., Vascepa Label, §§ 17.1.

Nor is the Clinical Studies section "merely describ[ing] exemplary effects of the drug" and amounting only to an "incidental reference" to an infringing use, as Defendants would have it. Defs' Br. at 12. Defendants' logic would categorically excluded the Clinical Study section of a label from the inducement analysis, which is once again contrary to Federal Circuit precedent.[14] For example, in *Sanofi v. Watson*, the Court's affirmance of an inducement finding expressly relied on expert testimony "that a person of ordinary skill in the art would read the drug label and understand that the only FDA-approved use of [the product] came out of the [clinical trial described in the label]". 875 F.3d at 645; *see also Vanda*, 887 F.3d at 1131 (relying on pharmacokinetic section of label to help show intent).

Even *Grunenthal GmbH v. Alkem Labs. Ltd.,* 919 F.3d 1333 (Fed. Cir. 2019), upon which Defendants (erroneously) rely, confirms the importance of the Clinical Studies section in informing the scope of the induced use. In *Grunenthal*, the patent was directed to management of neuropathic pain, and the generic defendants omitted the patent holder's indication for management of neuropathic pain from their prescribing information, seeking approval only for management of "severe chronic pain." *Id.* at 1339. In response to the argument that severe chronic pain could include neuropathic pain, the Federal Circuit observed that the generics had omitted not just the indication for neuropathic pain, but also all of the clinical studies in the Clinical Studies section concerning neuropathic pain. *Id.* at 1339–40. As the Court emphasized, the "proposed labels cite chronic lower back pain studies, a type of pain that Cross-Appellants and FDA defined as

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[14] [redacted] Peck Tr. 49:1–8 ("[A] physician . . . would manage a patient in the best interest of the patient according to the entire label. And would draw learning from every part of the label and employ that in the decision to treat."); *id.* at 50:11–21; *see also* Budoff Reply Report ¶¶ 31–37; Peck Rept. ¶ 199. In contrast, Defendants' expert expressly took an improperly limited and rigid view of which sections of the label can provide encouragement, suggestion, or recommendation to clinicians. Sheinberg Tr. 120:16–21 [redacted]

nociceptive [that is, non-neuropathic]." *Id.* *Grunenthal* thus confirms the relevance of the Clinical Studies section in understanding the scope of use induced by proposed labels.[15]

* * * * *

Defendants' product labels establish Defendants' intent to encourage, recommend, or suggest to clinicians that they administer Vascepa to their severely hypertriglyceridemic patients for at least 12 weeks. As the court in the strikingly similar *Sanofi v. Glenmark* case explained, the "additional clues in the labels that suggest long-term treatment, and the experts' testimony that prescribing physicians generally intend to treat patients with [the drug] for longer than [the claimed duration], together demonstrate by a preponderance of the evidence that Defendants' labels encourage administering the drug for at least [the claimed duration]." 204 F. Supp. 3d at 684. Here, the record contains testimony from both sides' experts confirming that Defendants' labels would induce administration for at least 12 weeks. To grant summary judgment on this issue would elevate Defendants' legally-incorrect and factually-unsupported arguments over Amarin's facts.

B. Defendants' Product Labels Will Induce Clinicians to Administer Their Generic Products to Treat Severe Hypertriglyceridemia and Achieve Specific Claimed Effects on TGs, LDL-C, and Apo B

Fourteen asserted claims also describe specific effects that—based on the clinical trial that formed the basis of FDA approval—clinicians expect when treating their severely hypertriglyceridemic patients with purified EPA. These claims recite one or more of the following effects: (a) a reduction in TGs that is either a specific percent (10%–25%) or statistically significant,

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[15] Defendants also wrongly rely on *Shire LLC v. Amneal Pharms., LLC*, No. 11-3781(SRC), 2014 WL 2861430, at *4–5 (D.N.J. June 23, 2014). *See* Defs.' Br. at 10–11. As ***the same judge*** later recognized, the *Shire* decision conflicts with Federal Circuit case law. *Impax Labs., Inc. v. Actavis Labs. FL, Inc.*, No. 15-6934(SRC), 2018 WL 1863826, at *10 (D.N.J. Apr. 18, 2018) ("Furthermore, the general argument that [the defendant] makes here is one that the Federal Circuit has rejected."); *see also id.* at *11–12 (discussing *AstraZeneca v. Apotex*, 633 F.3d at 1059–60 and *Eli Lilly*, 845 F.3d at 1368). Indeed, in *Impax*, the court denied the defendant's motion for summary judgment of noninfringement because "[a] reasonable finder of fact could also find that the label evidence, together with other circumstantial evidence, is sufficient for a finding that [the defendant] had the specific intent to induce infringement." *Impax*, 2018 WL 1863826, at *13. Accordingly, "[t]he question of specific intent to induce infringement is a matter for the finder of fact at trial." *Id.*

(b) no increase in LDL-C or no increase that is substantial, statistically significant, 5% or less, (c) a reduction in apo B or a statistically significant reduction in apo B. *See* Appendix B (listing the affected claims and the corresponding claim language).

The levels of these lipids play a critical role in the treatment of severe hypertriglyceridemia, *see* Peck Rept. ¶ 160, and that role is apparent from Defendants' own labels. For example, as explained in the Dosage and Administration section, doctors "[a]ssess lipid levels before initiating therapy." Vascepa Label, § 2. The Patient Information leaflet also states that clinicians will continue to monitor these lipid levels throughout treatment: "Your doctor may do blood tests to check your triglyceride and other lipid levels while you take VASCEPA." Vascepa Label, at 9–10; *see also* Peck Rept. ¶ 165. Mr. Mathers agreed that the Patient Information leaflet will reinforce the instruction elsewhere in the label "that the physician may do blood tests to check triglycerides and other lipid levels while the patient is taking Vascepa." Mathers Tr. 134:4–9.

As explained below, clinicians expect that each claimed effect will occur when treating severely hypertriglyceridemic patients using Defendants' products according to the claimed methods. As Defendants' expert explained, [redacted] Sheinberg Tr. 217:9–14; *accord* Budoff Tr. 152:3-6. Clinicians generally arrive at these expectations based on clinical study results. *See* Section V.A.2; *see also, e.g.*, Budoff Opening Rept. ¶¶ 63–64; Budoff Reply Rept. ¶¶ 33–36; Peck Tr. 154:3–5; Peck Rept. ¶¶ 221–225, 227. In this case, the relevant clinical study is the MARINE study, the results of which are described in the labels' Clinical Studies section. Based on that data, clinicians will expect that their severely hypertriglyceridemic patients will experience at least about a 25% reduction in TGs, and that this reduction will *not* be associated with a substantial increase in patients' LDL-C levels (or no rise at all). *See, e.g.*, Budoff Opening Rept. ¶¶ 143–49, 180–83; Budoff Reply Rept. ¶¶ 95–102, 114–29; Peck Rept. ¶¶ 226–29. Patients will also experience reductions in their apo B levels. Vascepa Label, § 14; *see also, e.g.*, Budoff Opening Rept. ¶¶ 241–42; Budoff Reply Rept. ¶¶ 141–51. Given these expectations, Defendants' labels are evidence of their intent that clinicians prescribe Vascepa to achieve these lipid results. Defendants' argument to the contrary should be rejected.

1. Defendants Labels Will Induce Clinicians to Use Defendants' Products to Reduce TGs By About 25%.

The Clinical Studies section encourages, recommends, or suggests to clinicians that they can expect a TG reduction that exceeds 25%: a 27% reduction in patients' TG levels compared to baseline (the patient's beginning TG level), and a 33% reduction in TGs compared to placebo control. Vascepa Label, § 14. This is the only data in the labels that clinicians can use to form their expectations, and this was the data that FDA found relevant to establishing how to safely and effectively use the drug. Budoff Tr. 147:4–8 [redacted]; *see also, e.g.*, Budoff Reply Rept. ¶¶ 98–102, 121; Peck Rept. ¶¶ 160–61, 221–25.

Defendants nonetheless argue that this data does not "predict icosapent's effects in a real-world patient," Defs.' Br. at 19. This argument is surprising, considering that (a) the clinical data was accepted by FDA as the basis for allowing Vascepa to be administered to patients; and (b) Defendants rely on the same data to get FDA approval for *their* products to be administered to patients. *See* Peck Rept. ¶¶ 89, 154–58. In any event, inducement does not require a showing that every patient who takes Vascepa experiences the exact same effects on lipids that appears in the label. Rather, it is enough that the label will "inevitably lead some physicians to infringe." *Eli Lilly*, 845 F.3d at 1369. Here, the MARINE data in the label is "median" data, meaning that just over half of the patients experienced a 27% reduction compared to baseline or greater and a 33% reduction compared to placebo. Vascepa Label, § 14; *see also, e.g.*, Budoff Opening Rept. ¶ 181; Budoff Reply Rept. ¶ 105. And as Dr. Sheinberg conceded, [redacted] Sheinberg Tr. 154:4–7. Accordingly, the median data reported in the label will inevitably lead some clinicians to infringe, which in turn demonstrates Defendants' intent to induce infringement of these claims. *See also* Budoff Tr. 152:18–24 [redacted] At a minimum, to the extent that the parties disagree about whether Vascepa's clinical study data, which Defendants

have adopted to obtain approval of their own generic products, accurately predicts Vascepa's real-world effects on a patient, that disagreement is a classic fact issue precluding summary judgment.

2. Defendants Labels Will Induce Clinicians to Use Defendants' Products to Treat Severe Hypertriglyceridemia and Expect Patients to Experience No Substantial Increase in LDL-C and a Reduction in Apo B

For essentially the same reasons reviewed above, the Clinical Studies section encourages, recommends, or suggests to clinicians to expect that after administering Defendants' products to severely hypertriglyceridemic patients for 12 weeks, those patients will experience approximately a 5% reduction in LDL-C compared to baseline and a 2% reduction compared to placebo control. Vascepa Label, § 14. Similarly, this section encourages, recommends, or suggests to clinicians to expect a 4% reduction in apo B compared to baseline and a 9% reduction compared to placebo control. Vascepa Label, § 14. Not only are these effects apparent from the data reported in the Clinical Studies section, but below the table, the labels specifically state that these effects will occur, and thus, encourage, recommend, or suggest that doctors should expect these effects. Vascepa Label, § 14. Experts on both sides agree with this reading.[16]

Defendants' attempt to diminish the importance of the data in the Clinical Studies section should be rejected for the reasons stated above. *See, e.g.*, *supra* Section V.A.2. Defendants also characterize the claimed effects on LDL-C and apo B as "off-label" uses, meaning that they are uses that are outside the approved indication for Defendants' products. *See* Defs.' Br. at 20–22. Defendants are incorrect.

The claimed LDL-C and apo B effects refer to additional treatment effects that clinicians

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[16] Budoff Tr. 151:22–24 [redacted] Sheinberg Tr. 168:11–19 [redacted] Mathers Tr. 154:5–12 ("Q: Some prescribers will understand the Vascepa labeling to tell them that they can administer Vascepa to their severely hypertriglyceridemic patients so as to reduce triglycerides without raising LDL-C, correct?" A: I think that's a fair prediction."); *see also* Peck Rept. ¶ 227.

should expect when administering the product in accordance with the approved label to reduce triglycerides in patients with severe hypertriglyceridemia. Defendants' own regulatory expert, Mr. Mathers, conceded that such use was *not* off-label. Mathers Tr. 156:11-18; *see also* Peck Rept. ¶¶ 228–35. Similarly, Defendants' expert Dr. Sheinberg was asked [redacted] Sheinberg Tr. 188:20–189:2. Dr. Sheinberg agreed [redacted] Sheinberg Tr. 189:13–18; *see also* Budoff Tr. 140:1–9 [redacted] Budoff Opening Rept. ¶ 147; Budoff Reply Rept. ¶ 116; Peck Rept. ¶¶ 226–27.

In this regard, Defendants mistakenly contend that the Federal Circuit's opinion in *Bayer v. Lupin* bars a finding of inducement for those claims that recite effects on LDL-C and apo B. *See* Defs.' Br. at 20. *Bayer* actually supports Amarin's position. The patent at issue in *Bayer* required administration to a patient *in need of* three separate effects. *Bayer*, 676 F.3d at 1319 ("1. A method of simultaneously achieving . . . a gestagenic effect, antiandrogenic effect, and an antialdosterone effect in a female patient in need thereof."). Thus, practicing the claimed method would require that a physician "determine that all three effects are needed by a specific . . . patient," and also meant that inducement required the label to contain an indication for all three effects. *Id.* at 1323–24. Defendants ignore that the *Bayer* court contrasted the claims in *Bayer* with claims that would "claim a method of achieving a[n indicated] effect in a patient in need of [the effect] in which the drug used to achieve [that effect] has *two generally beneficial additional effects*." *Id.* at 1323 (emphasis added). This describes the asserted claims in this case, which are directed to a method of achieving the indicated effect—reduction of TGs in a patient with severe hypertriglyceridemia—where the drug

(Defendants' products) also will have "two generally beneficial additional effects"—the absence of an increase in LDL-C and a reduction in apo B (depending on the claim at issue).

C. Defendants' Product Labels Will Induce Clinicians to Administer Their Generic Products to Severely Hypertriglyceridemic Patients Who Do Not Receive Concurrent Lipid Altering Therapy

Four of the fifteen asserted patent claims are directed to the treatment of severe hypertriglyceridemia with highly purified EPA where the patient "does not receive concurrent lipid altering therapy." *See* '728 Patent, Claims 1, 13, 16; '715 Patent, Claim 14. When, as here, a label describes that a drug is safe and effective for both monotherapy and combination therapy, then that label encourages, recommends, or suggests both. In fact, the Federal Circuit recently affirmed a finding of induced infringement (after a bench trial) where the label demonstrated that the drug was safe and effective as ***either*** monotherapy ***or*** in combination with "conventional therapy," but the patent claims covered only the combination therapy. *Sanofi*, 875 F.3d at 645 n.2. The district court found that the fact that "over half" of the patients were on combination therapy with conventional therapy and that the combination therapy "did not decrease positive outcomes . . . would encourage at least some physicians to administer [the drug]" in combination therapy. *Sanofi v. Glenmark*, 204 F. Supp. 3d at 683. Based on the label teaching both manners of administration, the district court concluded (and was affirmed), that "Defendants knew that their proposed labels would inevitably lead some physicians to administer [the drug in combination therapy]." *Id.* (quotation marks omitted).

Like the label at issue in *Sanofi*, Defendants' labels encourage, recommend, or suggest that clinicians will administer Defendants' products as adjunctive monotherapy or in combination therapy with an additional lipid altering therapy. Budoff Reply Rpt. ¶ 190; Budoff Tr. 165:15–17 [redacted]; Peck Tr. 49:16–19, 103:6–23; Peck Rept. ¶¶ 212–13. In particular, in the Clinical Studies section, the labels explain that "twenty-five percent of patients [in the MARINE Clinical Study] were on concomitant statin therapy" and thus clinicians appreciate that 75% of the study subjects were administered only Vascepa without any concurrent additional lipid-altering therapy. Vascepa Label, § 14. With or

without a statin, Vascepa was safe and effective. As Dr. Budoff explained, [redacted] Budoff Tr. 166:11–18; *see also* Peck Rept. ¶¶ 213–15. Defendants' experts agree that some clinicians will read the label as encouraging, recommending, or suggesting that they prescribe Defendants' products without a concurrent lipid altering therapy. Mathers Tr. 70:16–22 ("Q: So you would agree that some prescribers will follow the Vascepa labeling to administer their products to adult patients with severe hypertriglyceridemia who are not on a statin or other lipid-altering drug, correct? A: They could do that."); *see also* Sheinberg Tr. 207:17–208:18 [redacted] Thus, the language in Defendants' labels "would inevitably lead some physicians to infringe" the "without concurring lipid altering therapy" claims. *Eli Lilly*, 845 F.3d at 1369.

VI. FACT ISSUES REMAIN FOR TRIAL ON AMARIN'S CONTRIBUTORY INFRINGEMENT CLAIMS[17]

"Contributory infringement imposes liability on one who embodies in a non-staple device the heart of a patented process and supplies the device to others to complete the process and appropriate the benefit of the patented invention." *Vita-Mix Corp. v. Basic Holding, Inc.*, 581 F.3d 1317, 1327 (Fed. Cir. 2009). An ANDA filer contributorily infringes a method claim if the ANDA filer will, upon FDA approval, sell the product knowing it is especially made or especially adapted for use that infringes the patent claims, and the product is not a staple article or commodity of commerce suitable for substantial noninfringing use. 35 U.S.C. § 271(c). The patent owner need only establish by a preponderance of the evidence that (i) the ANDA filer had knowledge of the patent; (ii) the Proposed

[17] Plaintiffs do not oppose Defendants' Motion to the extent it relates to contributory infringement of the claims that require administration of EPA to patients who do not receive "concurrent lipid altering therapy." *See* '728 Patent, Claims 1, 13, 16; '715 Patent, Claim 14.

ANDA Product has no substantial noninfringing uses; and (iii) the Proposed ANDA Product is a material part of the invention described in the patent claims. *See Fujitsu Ltd. v. Netgear Inc.*, 620 F.3d 1321, 1326 (Fed. Cir. 2010).

Defendants contest the "substantial noninfringing use" and "especially made for or adapted" prongs, but contest these two prongs on the same basis. Defs.' Br. at 14–18, 23–24, 25–26. A substantial noninfringing use is one that is more than a use that is unusual, far-fetched, illusory, impractical, occasional, aberrant, or experimental. *Vita-Mix*, 581 F.3d at 1327. Determining whether a use is substantial takes into account not only the use's frequency, but the use's practicality, the invention's intended purpose, and the intended market. *i4i Ltd. P'ship*, 598 F.3d at 851 (upholding a verdict of contributory infringement despite three non-infringing ways of using accused code, based on evidence that those uses would deprive a user of the benefit of the accused feature). Conflicting expert testimony as to whether a noninfringing use is substantial often requires "weigh[ing] the testimony of all experts" and "ma[king] credibility determinations," thus precluding summary judgment. *See Grunenthal*, 919 F.3d at 1340–41; *see also Tyco Healthcare Grp. LP v. Biolitec, Inc.*, No. C-08-3129 MMC, 2010 WL 3324893, at *5 (N.D. Cal. Aug. 23, 2010) (denying motion for summary judgment on contributory infringement where there was competing expert testimony regarding whether a noninfringing use was "substantial").

A. Use of Defendants' Generic Products For Less Than 12 Weeks Is Not a Substantial Use

Like their induced infringement arguments, Defendants' attempt to avoid liability for contributory infringement is based on incorrect interpretations of the law and an incomplete depiction of expert deposition testimony. In particular, Defendants' arguments focus on whether their products have any noninfringing use. *See* Defs.' Br. at 14–18. Defendants would improperly erase "substantial" from the statute. Defendants arguments thus fail because they utilize the incorrect legal standard.

1. Defendants' Products Are Not "Suitable" for Noninfringing Use

The asserted claims are directed to the treatment of severe hypertriglyceridemia using 4

grams per day of highly purified EPA for at least 12 weeks. This is the same use for which Defendants seek approval. *See* Defs.' Br. at 7 (undisputed fact 3(a)). And, as explained in Section V.A.1, treatment of severe hypertriglyceridemia requires that the patient's TGs are reduced *and maintained* below 500 mg/dl to persistently avoid the risk of developing pancreatitis. *See, e.g.*, Fisher Tr. 72:4–8 (agreeing that indication refers to "keeping triglycerides below 500 milligrams per deciliter in a severely hypertriglyceridemic patient."). And, as also discussed above, clinicians recognize that the only way to accomplish this treatment is through long-term treatment (i.e., at least 12 weeks). *See supra* note 11. Accordingly, the uses described in the claims represent the only substantial use for Defendants' products. Upon approval, Defendants would supply those products for administration to patients, who will be treated with them according to the claims. Defendants' products thus "embod[y] . . . the heart of the patented process and suppl[y] [their products] to others to complete the process and appropriate the benefit of the patented invention." *Vita-Mix*, 581 F.3d at 1327.

Defendants nonetheless assert that Defendants' products are not "especially made" to be used for at least 12 weeks. Defs.' Br. at 15. Defendants ignore that their products will be especially made for the treatment of severe hypertriglyceridemia. Vascepa Label, § 1. And, expert deposition testimony establishes that the treatment of severe hypertriglyceridemia requires long-term therapy, and thus at least 12 weeks of therapy, to reduce and maintain TGs below 500 mg/dl. *See* Section V.A.1. In view of this testimony, other statements outside the label suggesting that the products will be suitable for reducing TGs in less than 12 weeks (Defs.' Br. at 16) are beside the point. The indication for Vascepa is directed to reducing and maintaining patients' TGs below 500 mg/dl. Thus, even assuming that Vascepa reduced TGs below 500 mg/dl in shorter than 12 weeks, treatment of this condition requires long-term therapy to *maintain* the TG reduction. *See supra* Section V.A.

Nor can Defendants' misreading of the patent specification, *see* Defs.' Br. at 15, support their argument. The specification simply notes that reductions in TGs begin about 1 week after the treatment with purified EPA begins. *See, e.g.*, '728 Patent, 3:65–4:6. The patent specification does not establish that a shorter duration of treatment will reduce TGs below 500 mg/dl, nor does it

demonstrate that a shorter duration will *keep* TGs below 500 mg/dl.

2. Any Noninfringing Use for Defendants' Products Is Not "Substantial"

Even if Defendants' products are "suitable" for shorter than 12-week treatment duration, such use is not "substantial." All parties' experts agree that when prescribing Vascepa for severely hypertriglyceridemic patients, clinicians' intend "indefinite" treatment. *See* Section V.A.1. It is difficult to imagine how a use that is contrary to how clinicians treat severely hypertriglyceridemic patients could be a "substantial" use. *See i4i Ltd. P'ship*, 598 F.3d at 851 ("In assessing whether an asserted noninfringing use was 'substantial,' the jury was allowed to consider not only the use's frequency, but also the use's practicality, the invention's intended purpose, and the intended market."). Defendants' attempt to show otherwise is based on cherrypicking Dr. Budoff's deposition testimony. *See* Defs.' Br. at 15. The testimony Defendants cite acknowledged only [redacted] Budoff Tr. 253:12–18. Dr. Budoff also testified, however, that [redacted][18] Defendants ignore the fact that their own clinical expert testified to the same effect. Sheinberg 134:24–135:8 [redacted]. Thus, taking into account the infrequency with which clinicians will use Defendants' products for less than 12 weeks, and clinicians' intent to use the products long term to persistently reduce severely hypertriglyceridemic patients' TG levels, there is no *substantial* noninfringing use for Defendants' products. *See i4i Ltd. P'ship*, 598 F.3d at 851.

B. Use of Defendants' Generic Products to Achieve Effects Other Than the Effects on TGs, LDL-C, and Apo B Recited in the Claims Are Not Substantial Uses

Defendants also argue that they will not contribute to clinicians infringing the fourteen claims

[18] Budoff Tr. 254:11–23 [redacted] *see also* Budoff Tr. 111:7–11 [redacted] Budoff Tr. 111:18–25 [redacted]

that recite specific effects on TGs, LDL-C, and apo B (*see* Appendix B) because, according to Defendants, a substantial number of patients will not experience effects consistent with these claim limitations. *See* Defs.' Br. at 23–24. As discussed above, more than half of the patients in the MARINE Clinical Study experienced lipid effects that exceeded the lipid effects in the claims. (*See supra* Section V.B). Although individual patients can respond to treatment in unexpected ways, clinicians' treating *intent* is to achieve similar effects in their patients. *See* Budoff Reply Rept. ¶¶ 104–09. For example, clinicians do not use Vascepa to cause an increase in their patients' LDL-C. Budoff Tr. 136:12–13 [redacted] *see also id.* 245:1–20. [redacted] Accordingly, when considering not only the frequency with which Vascepa is used to achieve effects other than those recited in the claims, but also the invention's intended purpose to achieve the effects described in the claims, Defendants cannot establish that they are entitled to judgment as a matter of law.

VII. CONCLUSION

For the foregoing reasons, Amarin respectfully requests that the Court deny Defendants' Motion for Summary Judgment of Noninfringement.

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Respectfully submitted,

/s/ Jason D. Smith

Nicholas J. Santoro (Nev. Bar No. 532)
Jason D. Smith (Nev. Bar No. 9691)
SANTORO WHITMIRE, LTD.
10100 W. Charleston Blvd., Suite 250
Las Vegas, NV 89135
Tel: (702) 948-8771 / Fax: (702) 948-8773
E-mail: nsantoro@santoronevada.com,
jsmith@santoronevada.com

Christopher N. Sipes (admitted *pro hac vice*)
Einar Stole (admitted *pro hac vice*)
Michael N. Kennedy (admitted *pro hac vice*)
Megan P. Keane (admitted *pro hac vice*)
Eric R. Sonnenschein (admitted *pro hac vice*)
Alaina M. Whitt (admitted *pro hac vice*)

Han Park (admitted *pro hac vice*)
Jordan L. Moran (admitted *pro hac vice*)
COVINGTON & BURLING LLP
One CityCenter, 850 Tenth Street, NW
Washington, DC 20001
Tel: (202) 662-6000 / Fax: (202) 662-6291
E-mail: csipes@cov.com, estole@cov.com, mkennedy@cov.com, mkeane@cov.com, esonnenschein@cov.com, awhitt@cov.com, hpark@cov.com, jmoran@cov.com

Attorneys for Plaintiffs Amarin Pharma, Inc. and Amarin Pharmaceuticals Ireland Limited

CERTIFICATE OF SERVICE

I hereby certify that on August 30, 2019, I caused true and correct copy of **AMARIN'S OPPOSITION TO DEFENDANTS' MOTION FOR SUMMARY JUDGMENT** to be filed with the Clerk of the Court using the Court's CM/ECF system, and service was thereby effected electronically to the following counsel of record in this matter and deposited for mailing in the U.S. Mail, postage prepaid and address to:

Wayne A. Shaffer
LAXALT & NOMURA, LTD.
9790 Gateway Drive, Suite 200
Reno, NV 89521
Tel: (775) 322-1170
Email: wshaffer@laxalt-nomura.com

George C. Lombardi
WINSTON & STRAWN LLP
35 W. Wacker Drive
Chicago, IL 60601
Tel: (312) 558-5969
Email: glombard@winston.com

Charles B. Klein
Claire A. Fundakowski
WINSTON & STRAWN LLP
1700 K Street N.W.
Washington, D.C. 20006
Tel: (202) 282-5000
Email: cklein@winston.com, cfundakowski@winston.com

Eimeric Reig-Plessis
WINSTON & STRAWN LLP
101 California Street
San Francisco, CA 94111
Tel: (415) 591-6808
Email: ereigplessis@winston.com

Attorneys for Defendants Hikma Pharmaceuticals USA, Inc. and Hikma Pharmaceuticals International Limited

Michael D. Rounds
Ryan James Cudnik
Brownstein Hyatt Farber Schreck, LLP
5371 Kietzke Lane
Reno, NV 89511
Email: mrounds@bhfs.com, rcudnik@bhfs.com

Constance S. Huttner
Frank D. Rodriguez
Caroline Sun
Beth Finkelstein
James Barabas
Windels Marx Lane & Mittendorf, LLP
1 Giralda Farms, First Floor
Madison, New Jersey 07940
Email: chuttner@ windelsmarx.com
frodriguez@ windelsmarx.com
csun@ windelsmarx.com
bfinkelstein@ windelsmarx.com
jbarabas@windelsmarx.com

Attorneys for Defendants Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd

/s/ Rachel Jenkins
An employee of Santoro Whitmire